

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (withdrawn amended) A dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising an extracellular region of an activating FcγR comprising an Fc binding site, joined to ~~a molecule~~ the Fc region of a human immunoglobulin that binds an FcRn, wherein said ~~molecule does not bind any FcγR~~ Fc region comprises one or more amino acid modifications that modulate one or more effector functions of the Fc region and wherein the dimeric fusion protein specifically binds an immune complex.

2. (withdrawn) The dimeric fusion protein of claim 1, wherein said activating FcγR is FcγRIIIA or FcγRIIA.

3. (currently amended) A dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising an extracellular region of an inhibitory FcγR comprising an Fc binding site, joined to ~~a molecule~~ the Fc region of a human immunoglobulin that binds an FcRn, wherein said ~~molecule does not bind any FcγR~~ Fc region comprises one or more amino acid modifications that modulate one or more effector functions of the Fc region and wherein the dimeric fusion protein specifically binds an immune complex.

4. (currently amended) The dimeric fusion protein of claim ~~1~~ 3, wherein said ~~molecule that binds an FcRn is the hinge constant region of immunoglobulin~~ is an IgG molecule.

5. (currently amended) The dimeric fusion protein of claim ~~4~~ 3, wherein said inhibitory FcγR is FcγRIIB.

6. (previously presented) The dimeric fusion protein of claim 4, wherein said IgG molecule is selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.

7. (withdrawn amended) A dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising an extracellular region of FcγRIIIA

comprising an Fc binding site, joined to a hinge-constant region of IgG2, wherein the IgG2 hinge-constant region comprises one or more amino acid modifications that modulate one or more effector functions of the IgG2 hinge-constant region and wherein the dimeric fusion protein specifically binds an immune complex.

8. (currently amended) A dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising an extracellular region of FcγRIIB comprising an Fc binding site, joined to a hinge-constant region of IgG2, wherein the IgG2 hinge-constant region comprises one or more amino acid modifications that modulate one or more effector functions of the IgG2 hinge-constant region and wherein the dimeric fusion protein specifically binds an immune complex.

9. (withdrawn amended) A method for treating, preventing or ameliorating one or more symptoms of an autoimmune disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of the dimeric fusion protein of claim 1-~~or~~ 3, or a pharmaceutically acceptable salt thereof.

10. (withdrawn) The method of claim 9, wherein said autoimmune disorder is idiopathic thrombocytopenic purpura, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Rieter's Syndrome, psoriasis, systemic lupus erythematosus, autoimmune hemolytic anemia, scleroderma, autoantibody triggered urticaria, pemphigus, vasculitic syndromes, Goodpasture's syndrome, multiple sclerosis, Sjogren's syndrome, Kawasaki's disease, polymyositis, or dermatomyositis.

11. (withdrawn) The method of claim 9 further comprising administering to said subject a therapeutically effective amount of one or more anti-inflammatory agents.

12. (withdrawn) The method of claim 9 further comprising administering to said subject a therapeutically effective amount of one or more immunomodulatory agents

13. (withdrawn amended) The method of claim 12, wherein at least one of said one or more immunomodulatory agent agents is a small organic molecule.

14. (withdrawn) The method of claim 13, wherein the small organic molecule is methotrexate, leflunomide, cyclophosphamide, cyclosporin A, FK506,

mycophenolate mofetil, rapamycin, mizoribine, deoxyspergualin, brequinar, malonitrolamide, steroid, or corticosteroid.

15. (withdrawn amended) The method of claim 11, wherein at least one of said one or more anti-inflammatory agents is a non-steroidal anti-inflammatory drug.

16. (withdrawn) The method of claim 15, wherein the non-steroidal anti-inflammatory drug is aspirin, ibuprofen, diclofenac, nabumetone, naproxen, or ketoprofen.

17. (withdrawn amended) A method of treating, preventing, or ameliorating one or more symptoms of idiopathic thrombocytopenic purpura, said method comprising administering to a subject in need thereof, a therapeutically effective amount of the dimeric fusion protein of claim ~~1~~ 3, in combination with administering to said subject a standard idiopathic thrombocytopenic purpura therapy.

18. (withdrawn amended) A method of treating, preventing, or ameliorating one or more symptoms of idiopathic thrombocytopenic purpura, said method comprising administering to a subject in need thereof, a therapeutically effective amount of the dimeric fusion protein of claim ~~1~~ 3, wherein said subject is refractory to a standard idiopathic thrombocytopenic purpura therapy.

19. (withdrawn) The method of claim 17 or 18, wherein said standard idiopathic thrombocytopenic purpura therapy is intravenous immunoglobulin therapy, corticosteroid therapy, splenectomy, or plasmapheresis.

20. (withdrawn) The method of claim 9, 17, or 18 wherein said subject is human.

21. (withdrawn) The method of claim 17 or 18, wherein said subject is immunocompromised.

22. (withdrawn) The method of claim 21, wherein said subject has cancer.

23. (currently amended) A pharmaceutical composition comprising a therapeutically effective amount of the dimeric fusion protein of claim ~~1~~ 3, and a pharmaceutically acceptable carrier.

24. (withdrawn) A dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising a variant extracellular region of FcγRIIIA joined to a hinge-constant region of IgG2, wherein said variant extracellular region comprises at least one amino acid modification relative to a wild-type extracellular region of FcγRIIIA, such that a 3G8 monoclonal antibody binds said dimeric fusion protein with a lower affinity than said monoclonal 3G8 antibody binds said wild-type extracellular region, and wherein the dimeric fusion protein specifically binds an immune complex.

25. (withdrawn) The dimeric fusion protein of claim 24, wherein said at least one amino acid modification in the extracellular region comprises a substitution in the 3G8 binding site of FcγRIIIA.

26. (withdrawn) The dimeric fusion protein of claim 25, wherein said 3G8 binding site is the BC loop of FcγRIIIA.

27. (withdrawn) The dimeric fusion protein of claim 25, wherein said 3G8 binding site is the FG loop of FcγRIIIA.

28. (withdrawn) The dimeric fusion protein of claim 24, wherein said at least one amino acid modification in the extracellular region of FcγRIIIA comprises a substitution at position 112 with aspartic acid, at position 113 with lysine, and at position 114 with proline.

29. (withdrawn) The dimeric fusion protein of claim 24, wherein said at least one amino acid modification in the extracellular region of FcγRIIIA comprises a substitution at position 160 with phenylalanine.

30. (withdrawn) The dimeric fusion protein of claim 24, wherein said at least one amino acid modification in the extracellular region of FcγRIIIA comprises a substitution at position 154 with asparagine and at position 155 with isoleucine.

31. (withdrawn) A dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising a variant extracellular region of FcγRIIIA joined to a hinge-constant region of IgG2, wherein said variant extracellular region comprises at least one amino acid modification relative to a wild-type extracellular region of FcγRIIIA, such that

an FcγRIIIA antibody binds said dimeric fusion protein with a lower affinity than said antibody binds said wild-type extracellular region, and wherein the dimeric fusion protein specifically binds an immune complex.

32. (withdrawn amended) A method for treating, preventing or ameliorating one or more symptoms of an autoimmune disorder, said method comprising administering to a subject in need thereof a therapeutically effective amount of the dimeric fusion protein of claim 24 ~~or 33~~ or 31, or a pharmaceutically acceptable salt thereof.

33. (withdrawn) A method for treating, preventing or ameliorating one or more symptoms of an autoimmune disorder, said method comprising administering to a subject in need thereof: (i) a therapeutically effective amount of a molecule which specifically binds a wild-type extracellular region of FcγRIIIA comprising an Fcγ binding site; and (ii) a therapeutically effective amount of a dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising a variant extracellular region of FcγRIIIA, wherein said variant extracellular region comprises at least one amino acid modification relative to said wild-type extracellular region, such that said molecule binds said dimeric fusion protein with a lower affinity than said molecule binds said wild-type extracellular region, and wherein said dimeric fusion protein specifically binds an immune complex.

34. (withdrawn) The method of claim 33, wherein said molecule is an antibody.

35. (withdrawn amended) The method of claim 34, wherein said antibody is CLB-GRAN1, BW2-9/2, GRM1, DJ130c, or LNK16.

36. (withdrawn) A method for treating, preventing or ameliorating one or more symptoms of an autoimmune disorder, said method comprising administering to a subject in need thereof (i) a therapeutically effective amount of the dimeric fusion protein of claim 24; and (ii) a therapeutically effective amount of a 3G8 monoclonal antibody or an antibody that competes with 3G8 for binding.

37. (withdrawn) The method of claim 36, wherein said 3G8 monoclonal antibody or an antibody that competes with 3G8 for binding is a humanized antibody.

38. (withdrawn) A method for treating, preventing or ameliorating one or more symptoms of an autoimmune disorder, said method comprising administering to a subject in need thereof: (i) a therapeutically effective amount of an antibody which specifically binds a wild-type extracellular region of FcγRIIB comprising an Fcγ binding site; and (ii) a therapeutically effective amount of a dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising a variant extracellular region of FcγRIIB, wherein said variant extracellular region comprises at least one amino acid modification relative to said wild-type extracellular region, such that said antibody binds said dimeric fusion protein with a lower affinity than said antibody binds said wild-type extracellular region, and wherein said dimeric fusion protein specifically binds an immune complex.

39. (withdrawn) The method of claim 38, wherein said antibody is produced by clone 2B6, having ATCC accession number PTA-459 1.

40. (withdrawn) The method of claim 38, wherein said antibody is produced by clone 3H7, having ATCC accession number PTA-4592.

41. (withdrawn) A method of treating, preventing, or ameliorating one or more symptoms of idiopathic thrombocytopenic purpura, said method comprising administering to a subject in need thereof, a therapeutically effective amount of the dimeric fusion protein of claim 24 or 33 in combination with administering to said subject a standard idiopathic thrombocytopenic purpura therapy.

42. (withdrawn) The method of claim 41, wherein said standard idiopathic thrombocytopenic purpura therapy is intravenous immunoglobulin therapy, corticosteroid therapy, splenectomy, or plasmapheresis.

43. (withdrawn) A method of treating, preventing, or ameliorating one or more symptoms of idiopathic thrombocytopenic purpura, said method comprising administering to a subject in need thereof, a therapeutically effective amount of the dimeric fusion protein of claim 24 in combination with a therapeutically effective amount of a 3G8 monoclonal antibody or an antibody that competes with 3G8 for binding.

44. (withdrawn) A method of treating, preventing, or ameliorating one or more symptoms of idiopathic thrombocytopenic purpura, said method comprising administering

to a subject in need thereof, a therapeutically effective amount of the dimeric fusion protein of claim 24 in combination with a therapeutically effective amount of a 3G8 monoclonal antibody, wherein said subject is refractory to a standard idiopathic thrombocytopenic purpura therapy.

45. (withdrawn) A method of treating, preventing, or ameliorating one or more symptoms of idiopathic thrombocytopenic purpura, said method comprising administering to a subject in need thereof, a therapeutically effective amount of the dimeric fusion protein of claim 24 in combination with a therapeutically effective amount of a 3G8 monoclonal antibody, wherein said method does not result in a side effect of standard idiopathic thrombocytopenic purpura therapy.

46. (withdrawn) The method of claim 45, wherein said side effect is neutropenia or cytokine release syndrome.

47. (withdrawn) The method of claim 43 further comprising administering to said subject a standard idiopathic thrombocytopenic purpura therapy.

48. (withdrawn) The method of claim 47, wherein said standard idiopathic thrombocytopenic purpura therapy is intravenous immunoglobulin therapy (IVIG).

49. (canceled)

50. (withdrawn) A pharmaceutical composition comprising: (i) a therapeutically effective amount of a molecule which specifically binds a wild-type extracellular region of FcγRIIIA comprising an Fcγ binding site; (ii) a therapeutically effective amount of a dimeric fusion protein comprising two identical polypeptide chains, each said chain comprising a variant extracellular region of FcγRIIIA, wherein said variant extracellular region comprises at least one amino acid modification relative to said wild-type extracellular region, such that said molecule binds said dimeric fusion protein with a lower affinity than said molecule binds said wild-type extracellular region, and wherein said dimeric fusion protein specifically binds an immune complex; and (iii) a pharmaceutically acceptable carrier.

51-55. (canceled)

56. (currently amended) An isolated polypeptide, comprising ~~an~~ the amino acid sequence of ~~one of~~ SEQ ID Nos No. 1-4, 34, 36, 38, 40, or 42.

57. (canceled)

58. (currently amended) An isolated polypeptide, comprising an amino acid sequence that is at least 75% homologous to and exhibits the same ligand binding and effector activity as the amino acid sequence ~~from any of SEQ ID Nos No. 1-4, 34, 36, 38, 40, and 42 and binds an immune complex but does not bind FcγRs.~~

59-60. (canceled)

61. (new) The dimeric fusion protein of claim 3, wherein said modulation of one or more effector functions of the Fc region is a reduction in interaction between said Fc region and one or more of FcγRIIA, FcγRIIIA and the C1q component of complement.

62. (new) The dimeric fusion protein of claim 8, wherein said modulation of one or more effector functions of the IgG2 hinge-constant region is a reduction in interaction between said IgG2 hinge-constant region and one or more of FcγRIIA, FcγRIIIA and the C1q component of complement.

63. (new) The dimeric fusion protein of claim 3, wherein said modification results in said Fc domain lacking effector function.

64. (new) The dimeric fusion protein of claim 8, wherein said modification results in the said IgG2 hinge-constant region lacking effector function.

65. (new) The dimeric fusion protein of claim 3, wherein the amino acid corresponding to position 297 in said Fc domain is not glycosylated.

66. (new) The dimeric fusion protein of claim 8, wherein the amino acid corresponding to position 297 in said IgG2 hinge-constant region is not glycosylated.

67. (new) The dimeric fusion protein of claim 65, wherein the amino acid corresponding to position 297 in said Fc domain is not asparagine.

68. (new) The dimeric fusion protein of claim 66, wherein the amino acid corresponding to position 297 in said IgG2 hinge-constant region is not asparagine.

69. (new) The dimeric fusion protein of claim 67, wherein the amino acid corresponding to position 297 in said Fc domain is glutamine.

70. (new) The dimeric fusion protein of claim 68, wherein the amino acid corresponding to position 297 in said IgG2 hinge-constant region is glutamine.

71. (new) The dimeric fusion protein of claim 3, wherein said Fc region comprises the mutation N297Q.

72. (new) The dimeric fusion protein of claim 8, wherein said IgG2 hinge-constant region comprises the mutation N297Q.